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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/048,035	06/11/2002	Wolf Bertling	10848-017001	1180

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EXAMINER	
BAUSCH, SARAE L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 12/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/048,035	BERTLING ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18-27 and 29-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18-27 and 29-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/03/2005 has been entered.

2. Currently, claims 1-16, 18-27, and 29-32 are pending in the instant application. Claims 17 and 28 have been canceled. Claims 29-32 are newly added. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented, or are reiterated from the previous office action. Response to arguments follow. This action is Non-FINAL.

Withdrawn Rejections

3. The rejections of claims 1 and 27, under 35 U.S.C. 112, second paragraph, made in section 5, page 2-3 of the previous office action, is withdrawn in view of the amendment to the claims.

4. The rejections of claims 1-4, 6, 8-9, 12-13, 20, 24, 26, and 27, under 35 U.S.C. 102(b), made in section 7, page 3 of the previous office action, is withdrawn in view of the amendment to the claims.

5. The rejections of claims 1-11, 13-15, 20, 24, 26, and 27 under 35 U.S.C. 102(b), made in section 8, pages 5-6 of the previous office action is withdrawn in view of the amendment to the claims.

6. The rejections of claims 1, 2, 6, 16, 18, 24, and 25, under 35 U.S.C. 102(b), made in section 10, page 9 of the previous office action is withdrawn in view of the amendment to the claims.

New Grounds of Rejections

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 7-10, 13-15, 18, 20-23, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Cantor et al (US Patent 5795714 Aug 1998).

Cantor et al. teach a method of replicating a probe array to screen biological samples for specific target sequences.

With regard to claim 1 and 27, Cantor et al. teach synthesizing one or more sets of nucleic acid probes simultaneously on a solid support (contacting (labeling) the substance (solid support) with at least one predefined nucleic acid molecule) (see column 8, lines 37-40). Cantor et al. teach a method comprising creating a set of nucleic acid probes (first group of predefined nucleic acid molecules), wherein each probe has a double stranded portion, a single stranded

portion, and a random sequence within the singe stranded portion (selecting at least one nucleic acid molecule) which is hybridized to a nucleic acid target (providing a second group of nucleic acid molecules with a detection sequence and contacting the substance (first group of predefined nucleic acid molecules attached to a solid support) with the nucleic acid molecules provided from the second group under predefined hybridization conditions) to the set of nucleic acid probes and determining the nucleotide sequence of the target which hybridized to the single stranded portion of any probe (detecting hybridization wherein hybridization identifies the substance) (see column 7, lines 11-20). Furthermore, Cantor et al. teach biotinylated double stranded probes (first nucleic acid group) attached to streptavidin coated beads adhered to polystyrene surface by spotting biotinylated compounds individually onto the streptavidin coated surface (predefined sites on substance, solid support) followed by hybridization of the target sequence to the probe by annealing and ligating the target sequence to the probe attached to the polystyrene beads (see column 20, lines 66-67, column 21, lines 1-8 and see column 31, lines 53-67) (second group of nucleic acid molecules bound to a predefined site on a solid surface).

With regard to claim 7-9, Cantor et al. teach attaching the nucleic acid probe to a solid support by immobilized 5'-labeled biotinylated DNA strands (coupling group, biotin) that consists of a variable 5 or 6 base segment plus the constant 15 base segment (see column 21, lines 59-66). The 5' labeled biotinylated DNA strand counteracts degradation caused by an exonuclease by protecting the 5' to exposure to the exonuclease.

With regard to claim 10, Cantor et al. teach the probe or the array of probes labeled with a fluorescent chemical (see column 9, lines 4-6 and lines 20-26).

With regard to claim 13 and 15, Cantor et al. teach one 5' end biotinylated strand of the probe duplex (predefined nucleic acid molecule) is attached to a solid surface (see column 19, lines 34-40) and teach moderately dense arrays can be made using a typical X-Y robot to spot the biotinylated compounds individually (predefined nucleic acid molecules) onto a streptavidin coated surface (particle) and streptavidin-coated beads can be adhered, permanently to plastics like polystyrene (instant claim 15) (see column 20, lines 65-67, column 21 lines 1-9).

With regard to claim 18, Cantor et al. teach a labeled probe or target molecule with a fluorescent chemical that may be directly or indirectly detected using scintillation fluid or a PhosphorImager, chromatic or fluorescent labeling or mass spectrometry (see column 9, lines 4-7 and lines 14-26) (complementary detection sequence detected by means of fluorescence).

With regard to claim 20, Cantor et al. teach the nucleic acids may be artificially synthesized (see column 6, lines 43-47).

With regard to claim 21 and 22, Cantor et al. teach the set of nucleic acid probes (first group of nucleic acid molecules) and target nucleic acid (second group of nucleic acid molecules) comprise PNA (nucleic acid analog) (see column 7, lines 20-24).

With regard to claim 23, Cantor et al. teach a target nucleic acid hybridized to a probed attached to a solid support, such as plastic, ceramic, metal, resin, film or other polymer, gel, membrane, or two or three dimensional array such as a chip or microchip (see column 12, lines 56-67).

Response to Arguments

9. The response traverses the rejection on page 9-10 of the response mailed 10/03/2005. The response asserts on page 10, first paragraph of the response that the nucleic acids having a

random sequence, taught by Cantor et al, would not be used in this claimed methods. The response asserts that the random sequence nucleic acids would not allow for identification of a substance as the pending claims recite. The response asserts that the claims indicate that nucleic acid sequence are "predefined" and "predefined" can be interpreted to mean "nonrandom". This response has been thoroughly reviewed but not found persuasive because the claims do not require that the sequence is not random. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., predefined sequences meaning nonrandom sequences) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims do not require that sequence is non-random, the claims only require that the nucleic acid is predefined. A predefined nucleic acid molecule does not mean that the sequence of the nucleic acid is known or non-random, predefined means to define beforehand and the claim only requires that the nucleic acid molecule is defined beforehand. This could be interpreted to mean any group of nucleic acids which are selected to be used in the assay are "predefined nucleic acid molecules" therefore the cited reference does teach the claimed method of labeling and identifying a solid, liquid or gaseous substance using predefined nucleic acid molecules.

10. The response asserts that a random sequence nucleic acid molecule would not allow for identification of a substance as the pending claims recite. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., identification of the substance) are not recited in the

rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims do not require that identification of a substance occurs, the claims require only that IF hybridization of occurs then the substance occurs. The claims recite a final process step of when hybridization does not occur between the IDS1-n of all of said selected nucleic acid molecules and said IDP1-n of said second group of nucleic acid molecules, the substance is not identified. Therefore the claim does not require that the substance be identified and therefore the cited reference does teach the claimed method.

11. The response further asserts that claims 2-4 are direction toward primer binding sites and Cantor et al. makes no suggestion of two primer binding sections. This response has been thoroughly reviewed but not found persuasive because claims 2-4 were not rejected under 35 USC 102(b) as being anticipated by Cantor et al.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-15, 18-23, 27, 29-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Lizardi et al. (US Patent 5854033, Dec 29, 1998).

With regard to claim 1, 6-9, 13-15, 19, 23, 27, and 29-32, Lizardi et al. teach a method

for detection of target nucleic acid sequences (see column 5, lines 1-3) (identification of substance). Lizardi et al. teach mixing an open circle probe (selecting a predefined nucleic acid molecule with an identification sequence section) with a target (substance) sample and incubating the probe with the target sample to promote hybridization (contacting with nucleic acid molecule and labeling the substance) (see column 19, lines 30-50) followed by amplification (claim 6). Lizardi et al. teach the amplified nucleic acid labeled by incorporation of biotin-16-UTP (claim 7-9, 13-15) can be detected by immobilizing the nucleic acid on a solid glass surface (claim 23) by hybridization with a complementary DNA oligonucleotide (address probe) complementary to the target sequence present in the amplified nucleic acid (claim 6) (second group of nucleic acid molecules comprising complementary identification sequence and bound to a predefined site on a solid surface) and detecting hybridization (identifying substance) (see column 23, lines 35-52). Lizardi et al. further teach melting temperatures of target sequence (identification sequence) that are identical to the probe sequence as well as with small modifications (see column 32, lines 44-67) (claims 29-30).

With regard to claims 2-6, Lizardi et al. teach identification sections are located between two primer binding sequence sections, are complementary to each other and have the same melting point (see figure 1-3) (see column 6, lines 5-25).

With regard to claim 10-12 and 18 Lizardi et al. teach detection probes are labeled to oligonucleotides having sequence complementary to detection tags on TS-DNA and are preferable molecular beacons, probes labeled with fluorescent moieties (see column 11, lines 45-65).

With regard to claim 20, Lizardi et al. teach that the probes and primers can be synthesized using established oligonucleotide synthesis methods (see column 13, lines 60-68 and column 14, lines 1-16).

With regard to claim 21-22, Lizardi et al. teach peptide nucleic acid analogs can be used for both the right and left target probe (see column 13, lines 40-58).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1,2, 6, 16, 18, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bumstead et al. (J. Virological Methods 65 (1997) 75-81) in view of Pastinen et al. (Human Mol. Genetics 13 (1998) vol. 7 pp. 1453-1462).

Bumstead et al. teach a quantitative assay to determine the number of viral genomes present in samples by PCR amplification of the viral genome using fluorescent-tagged primers (abstract). Bumstead et al. teach 2µl cells (first group of predefined nucleic acid molecules) in a volume of 25ml PCR reaction (substance, thereby labeling substance) with 10pmol of primer (second group of nucleic acid molecules, wherein each nucleic acid molecule comprises a detection sequence section complementary to one of the identification sequences and contacting the substance with the nucleic acid molecules under predefined hybridization conditions). Bumstead et al. teach primers used to detect MDV to amplify a product of 279 bp (identification sequence of the predefined nucleic acid molecules). Bumstead et al. teach amplification of the

PCR reaction and quantification of products of PCR by electrophoresis on a sequencer (detecting hybridization and identifying the substance). (see section 2.2 page 76-77). Bumstead et al. teach primers used to amplify a product of 279 bp (identification sequence located between two primer binding sequence sections). (see section 2.2 page 76) (claim 2). Bumstead et al. teach amplification of product 279 of MDV by two primers by PCR. (see section 2.2 page 76-77) (claim 6 and 24). Bumstead et al. teach amplification of Marek's disease virus (particle), a herpes virus (abstract), from cells by PCR. The cells contain MDV and were not purified. The MDV contains the 279 bp region of the MDV genome. Bumstead teaches a particle (MVD virus) that is a virus-like particle included in the predefined nucleic acid molecule (MVD genome) (1st paragraph, 2nd column, page 76 and section 2.2, page 76-77). Bumstead et al. teach quantification of the fluorescent bands from the PCR products by ABI Genescna software (detection by fluorescence of the hybridization of the identification sequence section with the complementary detection sequence section) (see 1st paragraph, 1st column, page 77) (claim 18). Bumstead et al. teach the use of fluorescently labeled primer, primer 1 (1st paragraph, section2.2, page 76) (claim 25). Bumstead et al. does not teach a second set of nucleic acid molecules on a solid support.

Pastinen et al. teach an array-based multiplex analysis of candidate genes (see abstract). Pastinen et al. teach microscopic glass slide with 12 wells were treated and 12 detection primers were printed in each of the 12 wells (see array preparation, page 1460). Pastinen et al. teach PCR amplification and identification of substance by hybridization of PCR product on array (see page 1460, minisequencing reactions on primer array and signal detection). Pastinen et al. teach multiplex genotyping and miniaturized assay format has the advantage of small reaction

volumes, fast reaction rates, and easy handling of multiple samples in parallel (see page 1451, 2nd column, last paragraph).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of determine the number of viral genomes present in samples by PCR amplification of the viral genome using fluorescent-tagged primers by Burman et al. to include array analysis, as taught by Pastinen, to improve the method by Burman et al.. The ordinary artisan would have been motivated to improve the method of determining the number of viral genomes present in a sample by using PCR amplification and hybridization detection by Burman et al. with the method of array analysis by Pastinen et al. because Pastinen teaches multiplex genotyping and miniaturized assay format has the advantage of small reaction volumes, fast reaction rates, and easy handling of multiple samples in parallel. The ordinary artisan would have had a reasonable expectation of success that the use of array analysis could be used in the method of Burman et al. because both Burman et al. and Pastinen et al. using PCR amplification to identify genes and Pastinen et al. teach that PCR amplification and identification of substance by hybridization of PCR product on array allows for easy handling of multiple samples in parallel.

Conclusion

15. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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